Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptansc1625

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	JUL 02	LMEDLINE coverage updated
NEWS 3	JUL 02	SCISEARCH enhanced with complete author names
NEWS 4	JUL 02	CHEMCATS accession numbers revised
NEWS 5	JUL 02	CA/CAplus enhanced with utility model patents from China
NEWS 6	JUL 16	CAplus enhanced with French and German abstracts
NEWS 7	JUL 18	CA/CAplus patent coverage enhanced
NEWS 8	JUL 26	USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 9	JUL 30	USGENE now available on STN
NEWS 10	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS 11	AUG 06	BEILSTEIN updated with new compounds
NEWS 12	AUG 06	FSTA enhanced with new thesaurus edition
NEWS 13	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS 14	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS 15	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS 16	AUG 27	USPATOLD now available on STN
NEWS 17	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS 18	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 19	SEP 13	FORIS renamed to SOFIS
NEWS 20	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS 21	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS 22	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS 23	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific

research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 18:36:31 ON 28 SEP 2007

=> fil casreact

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'CASREACT' ENTERED AT 18:36:44 ON 28 SEP 2007
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications.

FILE CONTENT:1840 - 22 Sep 2007 VOL 147 ISS 14

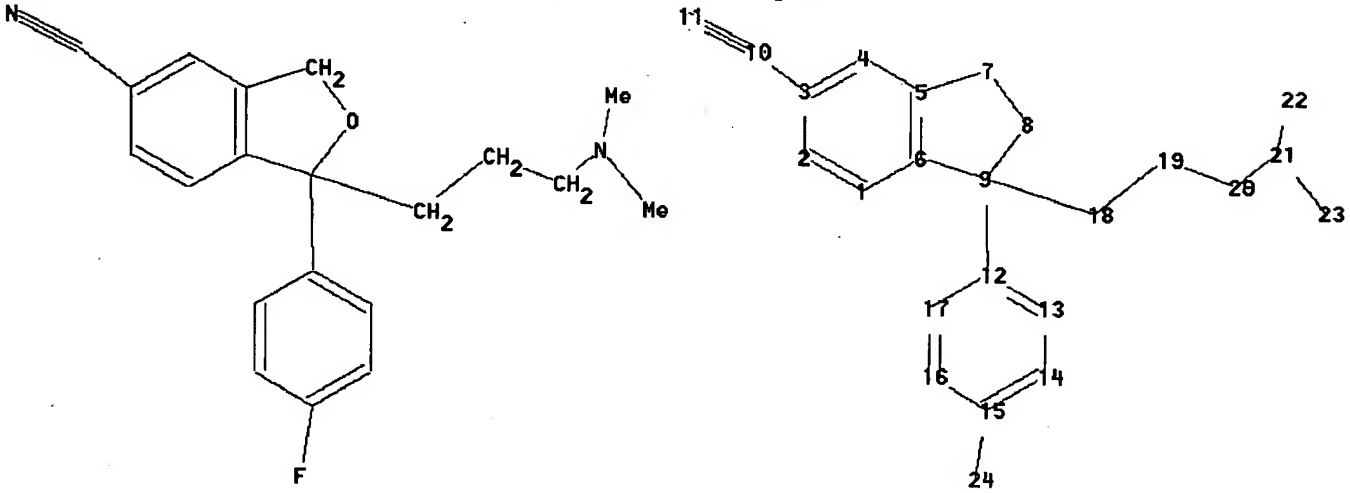
New CAS Information Use Policies, enter HELP USAGETERMS for details.

****
*
* CASREACT now has more than 12 million reactions *
*
****

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>
Uploading C:\Program Files\Stnexp\Queries\citalopramA.str



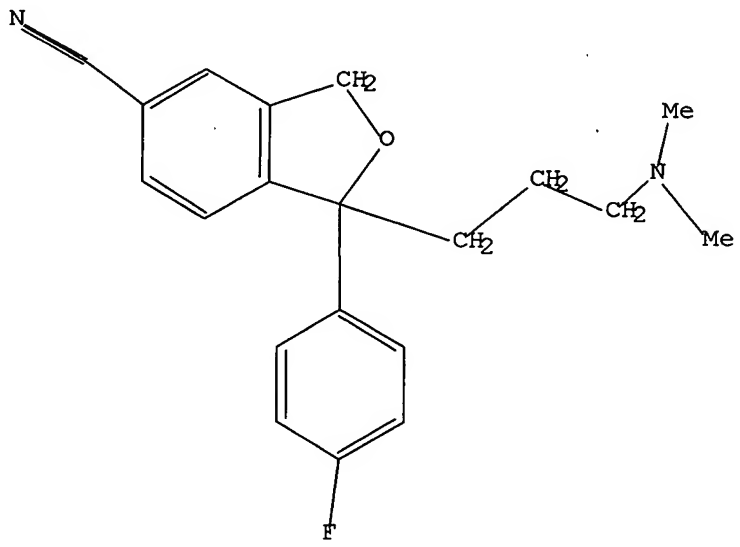
chain nodes :
10 11 18 19 20 21 22 23 24

ring nodes :
1 2 3 4 5 6 7 8 9 12 13 14 15 16 17
chain bonds :
3-10 9-12 9-18 10-11 15-24 18-19 19-20 20-21 21-22 21-23
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 12-13 12-17 13-14 14-15 15-16
16-17
exact/norm bonds :
5-7 6-9 7-8 8-9 10-11
exact bonds :
3-10 9-12 9-18 15-24 18-19 19-20 20-21 21-22 21-23
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 12-13 12-17 13-14 14-15 15-16 16-17

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS
fragments assigned product role:
containing 1

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s sss sam l1
SAMPLE SEARCH INITIATED 18:37:54 FILE 'CASREACT'
SCREENING COMPLETE - 28 REACTIONS TO VERIFY FROM 5 DOCUMENTS

100.0% DONE 28 VERIFIED 28 HIT RXNS 5 DOCS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED VERIFICATIONS: 243 TO 877
PROJECTED ANSWERS: 5 TO 234

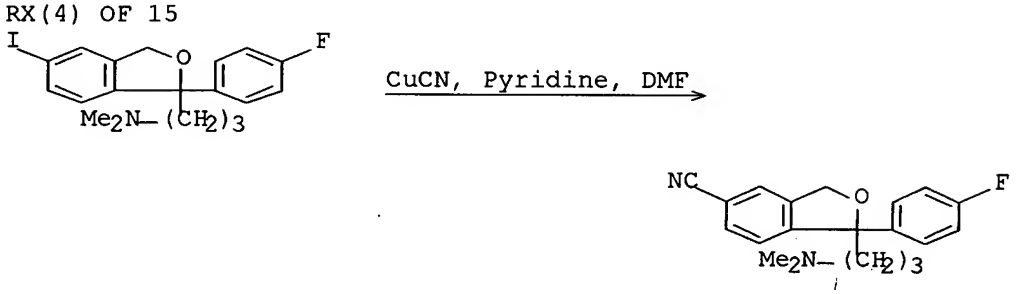
L2 5 SEA SSS SAM L1 (28 REACTIONS)

=> d scan

L2 5 ANSWERS CASREACT COPYRIGHT 2007 ACS on STN

TI Processes for the preparation of citalopram and its intermediate from 5-aminophthalide

RX(4) OF 15



ALL ANSWERS HAVE BEEN SCANNED

=> fil stng
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.35	1.56

FILE 'STNGUIDE' ENTERED AT 18:38:21 ON 28 SEP 2007
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Sep 24, 2007 (20070924/UP).

=> s sss l1 full
SUBSTANCE QUERIES NOT VALID IN THIS FILE
The logic expression entered contains L#s or saved query names which correspond to structures built by the STRUCTURE command or to screen sets. These must be searched in a substance file such as the REGISTRY file. In some files you may use a Registry Number answer set from a structure search as a search term or profile in some bibliographic file containing Registry Numbers, e.g. the CA file. For an explanation, enter "HELP CROSSOVER" at an arrow prompt (=>).

=> fil casreact
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.90	2.46

FILE 'CASREACT' ENTERED AT 18:47:09 ON 28 SEP 2007

FILE CONTENT:1840 - 22 Sep 2007 VOL 147 ISS 14

New CAS Information Use Policies, enter HELP USAGETERMS for details.

****
*
* CASREACT now has more than 12 million reactions
*
****

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

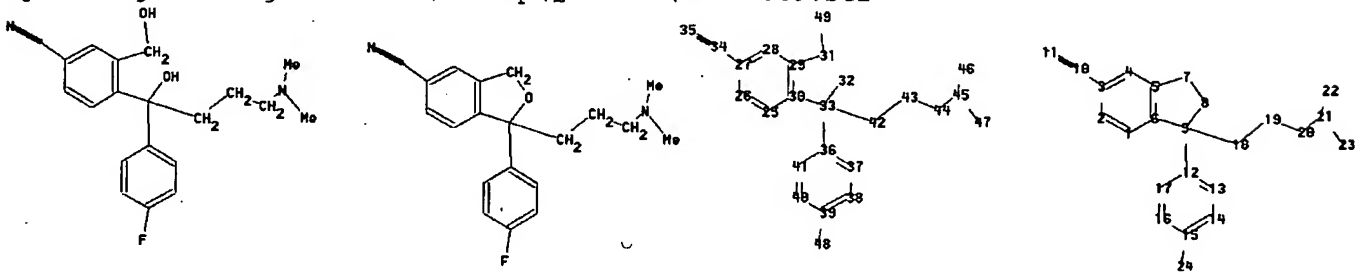
=> s sss l1 full
FULL SEARCH INITIATED 18:47:24 FILE 'CASREACT'
SCREENING COMPLETE - 323 REACTIONS TO VERIFY FROM 76 DOCUMENTS

100.0% DONE 323 VERIFIED 271 HIT RXNS 72 DOCS
SEARCH TIME: 00.00.01

L3 72 SEA SSS FUL L1 (271 REACTIONS)

=> save l3 citalopram07/A
ANSWER SET L3 HAS BEEN SAVED AS 'CITALOPRAM07/A'

=>
Uploading C:\Program Files\Stnexp\Queries\10577869.str



chain nodes :
10 11 18 19 20 21 22 23 24 31 32 33 34 35 42 43 44 45 46 47 48 49
ring nodes :
1 2 3 4 5 6 7 8 9 12 13 14 15 16 17 25 26 27 28 29 30 36 37 38 39 40 41
chain bonds :
3-10 9-12 9-18 10-11 15-24 18-19 19-20 20-21 21-22 21-23 27-34 29-31 30-33 31-49 32-33 33-36 33-42 34-35 39-48 42-43 43-44 44-45 45-46 45-47
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 12-13 12-17 13-14 14-15 15-16

16-17 25-26 25-30 26-27 27-28 28-29 29-30 36-37 36-41 37-38 38-39 39-40
40-41
exact/norm bonds :
5-7 6-9 7-8 8-9 10-11 32-33 34-35
exact bonds :
3-10 9-12 9-18 15-24 18-19 19-20 20-21 21-22 21-23 27-34 29-31 30-33
31-49 33-36 33-42 39-48 42-43 43-44 44-45 45-46 45-47
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 12-13 12-17 13-14 14-15 15-16 16-17 25-26 25-
30 26-27 27-28 28-29 29-30 36-37 36-41 37-38 38-39 39-40 40-41

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:Atom 26:Atom 27:Atom
28:Atom 29:Atom 30:Atom 31:Atom 32:Atom 33:Atom 34:CLASS 35:CLASS 36:Atom
37:Atom 38:Atom 39:Atom 40:Atom 41:Atom 42:CLASS 43:CLASS 44:CLASS 45:CLASS
46:CLASS 47:CLASS 48:CLASS 49:CLASS
fragments assigned product role:
containing 1
fragments assigned reactant/reagent role:
containing 25

L4 STRUCTURE UPLOADED

=> d l4
L4 HAS NO ANSWERS
L4 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l4 sss subset=l3 sam
SAMPLE SUBSET SEARCH INITIATED 18:49:07 FILE 'CASREACT'
SCREENING COMPLETE - 0 REACTIONS TO VERIFY FROM 0 DOCUMENTS

100.0% DONE 0 VERIFIED 0 HIT RXNS 0 DOCS
SEARCH TIME: 00.00.01

PROJECTIONS (WITHIN SPECIFIED SUBSET): ONLINE **COMPLETE**
PROJECTED VERIFICATIONS (WITHIN SPECIFIED SUBSET): 0 TO 0
PROJECTED ANSWERS (WITHIN SPECIFIED SUBSET): 0 TO 0

L5 0 SEA SUB=L3 SSS SAM L4 (0 REACTIONS)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> d his

(FILE 'HOME' ENTERED AT 18:36:31 ON 28 SEP 2007)

FILE 'CASREACT' ENTERED AT 18:36:44 ON 28 SEP 2007

```
L1              STRUCTURE UPLOADED
L2            5 S SSS SAM L1

     FILE 'STNGUIDE' ENTERED AT 18:38:21 ON 28 SEP 2007

     FILE 'CASREACT' ENTERED AT 18:47:09 ON 28 SEP 2007
L3           72 S SSS L1 FULL
                SAVE L3 CITALOPRAM07/A
L4              STRUCTURE UPLOADED
L5            0 S L4 SSS SAM SUB=L3

=> s l4 subset=l3 sam
SAMPLE SUBSET SEARCH INITIATED 18:50:44 FILE 'CASREACT'
SCREENING COMPLETE -        0 REACTIONS TO VERIFY FROM        0 DOCUMENTS

100.0% DONE       0 VERIFIED       0 HIT RXNS                      0 DOCS
SEARCH TIME: 00.00.01

PROJECTIONS (WITHIN SPECIFIED SUBSET):          ONLINE  **COMPLETE**
PROJECTED VERIFICATIONS (WITHIN SPECIFIED SUBSET):       0 TO        0
PROJECTED ANSWERS (WITHIN SPECIFIED SUBSET):             0 TO        0

L6            0 SEA SUB=L3 SSS SAM L4 (     0 REACTIONS)

=> s l4 subset=l3 full
FULL SUBSET SEARCH INITIATED 18:51:16 FILE 'CASREACT'
SCREENING COMPLETE -       44 REACTIONS TO VERIFY FROM       17 DOCUMENTS

100.0% DONE      44 VERIFIED      27 HIT RXNS                     14 DOCS
SEARCH TIME: 00.00.01

L7           14 SEA SUB=L3 SSS FUL L4 (    27 REACTIONS)

=> d ibib abs hit 1-14


L7   ANSWER 1 OF 14  CASREACT  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:        147:211613  CASREACT  Full-text
TITLE:                   Process for asymmetric alkylation of carbonyl
                         compounds
INVENTOR(S):             Albert, Martin; Sturm, Hubert; Berger, Andreas;
                         Kremminger, Peter
PATENT ASSIGNEE(S):      Sandoz A.-G., Switz.
SOURCE:                  PCT Int. Appl., 36pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2007082771      A1   20070726       WO 2007-EP516    20070122
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN,
             KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK,
             MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO,
             RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,
             TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
```

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

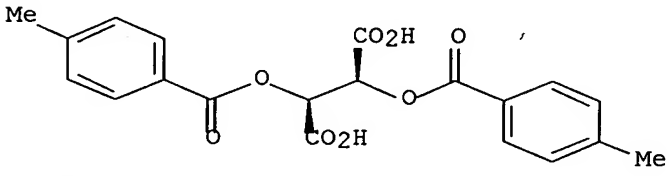
PRIORITY APPLN. INFO.: GB 2006-1286 20060123

OTHER SOURCE(S): MARPAT 147:211613

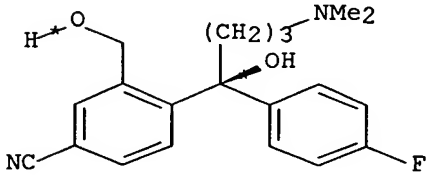
AB This invention relates to a process for stereoselective alkylation of carbonyl groups comprising reaction of a carbonyl compound (containing an anchor group capable of reacting with a boric or boronic acid derivs.) with an organometallic compound in the presence of a chiral alc. and a boron compound For example, 4-(4-fluorobenzoyl)-3-(hydroxymethyl)benzonitrile was reacted with (1S,2S)-N-methylpseudoephedrine and diisopropoxymethylborane, followed by the addition of dimethylaminopropyl magnesium chloride to give (S)-4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxy-1-butyl]-3-(hydroxymethyl)benzonitrile with 90.0% enantiomeric excess. The chiral tertiary alc. obtained in the previous step is an useful intermediate for synthesizing antidepressant drug Escitalopram.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

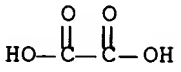
RX(8) OF 24 ...D + Y ===> Z



D: CM 1

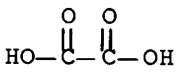


D: CM 2

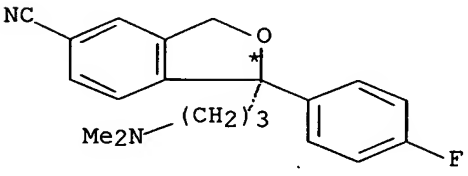


Y

(8)



Z: CM 1



Z: CM 2

RX(8) RCT D 128173-53-5

STAGE(1)
RGT AA 7664-41-7 NH3
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON room temperature, pH 9

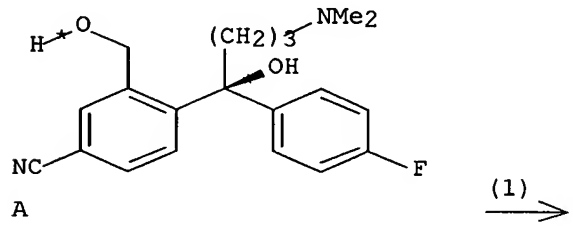
STAGE(2)
RGT AB 121-44-8 Et3N, AC 104-15-4 TsOH
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1 hour, <5 deg C

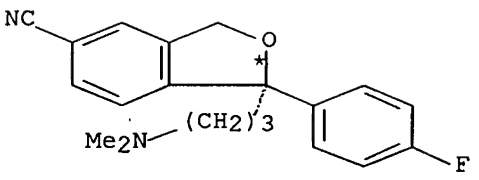
STAGE(3)
RCT Y 144-62-7

PRO Z 219861-08-2
NTE stereoselective

L7 ANSWER 2 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 146:500809 CASREACT Full-text
TITLE: An improved resolution process for the preparation of antidepressant drug: escitalopram
AUTHOR(S): Mital, Alka; Kumar, Rakesh; Ramachandran, Uma
CORPORATE SOURCE: Department of Pharmaceutical Technology, National Institute of Pharmaceutical Education and Research (NIPER), Mohali, 160062, India
SOURCE: Organic Preparations and Procedures International (2006), 38(4), 423-426
CODEN: OPPIAK; ISSN: 0030-4948
PUBLISHER: Organic Preparations and Procedures, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Efficient resolution process for the intermediate racemic diol 4-(4-dimethylamino)-1-(4'-fluorophenyl)-1-(hydroxybutyl)-3-(hydroxymethyl)benzonitrile, wherein the S-diol is obtained in pure form, which is basified and then cyclized to give S-citalopram of >99 % enantiomeric purity. The method provides an easy way to improve the enantiomeric purity of S-citalopram that is obtained by diastereomeric salt crystallization method as compared to the other processes. The novelty of this process is that the enriched diastereomeric salt is crystallized twice using a medium polar solvent, before it is released as a free base. This avoids the cumbersome two stage purification process of the other reported processes.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 10 ...A ===> B

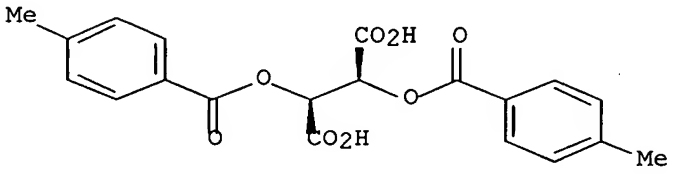




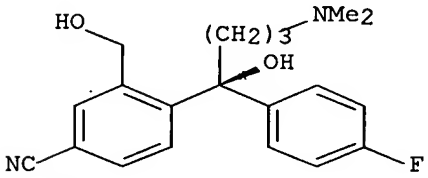
B
YIELD 70%

RX(1) RCT A 488787-59-3
RGT C 121-44-8 Et3N, D 124-63-0 MeSO2Cl
PRO B 128196-01-0
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 10 minutes, 0 deg C
SUBSTAGE(2) 3 hours, 0 deg C

RX(7) OF 10 COMPOSED OF RX(4), RX(1)
RX(7) K ===> B

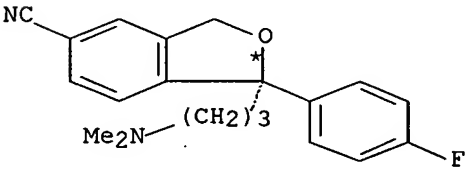


K: CM 1



K: CM 2

2
STEPS

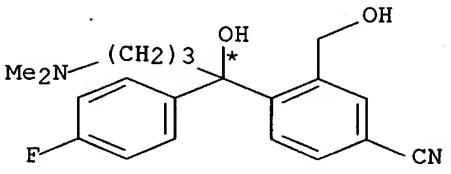


B
YIELD 70%

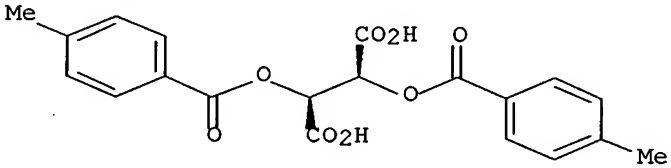
RX(4) RCT K 128173-53-5
       RGT M 144-55-8 NaHCO3
       PRO A 488787-59-3
       SOL 7732-18-5 Water
       CON room temperature

RX(1) RCT A 488787-59-3
       RGT C 121-44-8 Et3N, D 124-63-0 MeSO2Cl
       PRO B 128196-01-0
       SOL 108-88-3 PhMe
       CON SUBSTAGE(1) 10 minutes, 0 deg C
            SUBSTAGE(2) 3 hours, 0 deg C

RX(9) OF 10 COMPOSED OF RX(3), RX(4), RX(1)
RX(9) G + J ===> B

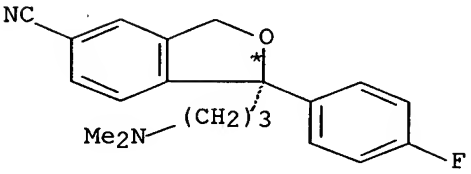


G



J

3 STEPS →



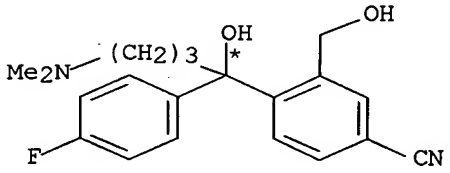
B
YIELD 70%

RX(3) RCT G 103146-25-4, J 32634-68-7
       PRO K 128173-53-5
       SOL 67-63-0 Me2CHOH
       CON 5 hours, 40 deg C

RX(4) RCT K 128173-53-5
RGT M 144-55-8 NaHCO3
PRO A 488787-59-3
SOL 7732-18-5 Water
CON room temperature

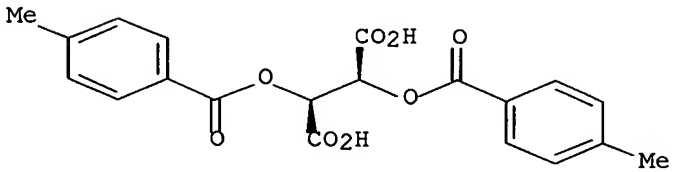
RX(1) RCT A 488787-59-3
RGT C 121-44-8 Et3N, D 124-63-0 MeSO2Cl
PRO B 128196-01-0
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 10 minutes, 0 deg C
SUBSTAGE(2) 3 hours, 0 deg C

RX(10) OF 10 COMPOSED OF RX(2), RX(3), RX(4), RX(1)
RX(10) F + J ===> B



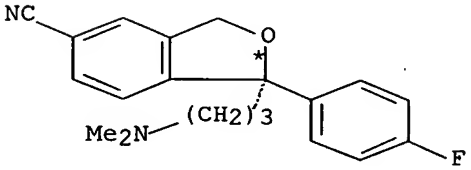
● HBr

F



J

4
STEPS



B
YIELD 70%

RX(2) RCT F 103146-26-5

RGT H 1310-73-2 NaOH
PRO G 103146-25-4
SOL 7732-18-5 Water, 108-88-3 PhMe
CON 15 minutes, 0 deg C

RX(3) RCT G 103146-25-4, J 32634-68-7
PRO K 128173-53-5
SOL 67-63-0 Me2CHOH
CON 5 hours, 40 deg C

RX(4) RCT K 128173-53-5
RGT M 144-55-8 NaHCO3
PRO A 488787-59-3
SOL 7732-18-5 Water
CON room temperature

RX(1) RCT A 488787-59-3
RGT C 121-44-8 Et3N, D 124-63-0 MeSO2Cl
PRO B 128196-01-0
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 10 minutes, 0 deg C
SUBSTAGE(2) 3 hours, 0 deg C

L7 ANSWER 3 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 146:206191 CASREACT Full-text
TITLE: An improved process for preparation of escitalopram
INVENTOR(S): Kaushik, Vipin Kumar; Khan, Mohammed Umar; Meenakshisunderam, Sivakumaran
PATENT ASSIGNEE(S): Aurobindo Pharma Limited, India
SOURCE: PCT Int. Appl., 18pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

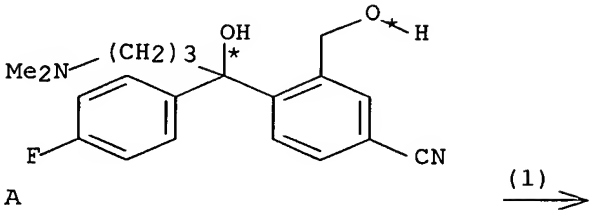
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007012954	A1	20070201	WO 2006-IB2050	20060720
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
IN 2005CH01014	A	20070720	IN 2005-CH1014	20050727

PRIORITY APPLN. INFO.: IN 2005-CH1014 20050727

AB The present invention relates to an improved process for the preparation of escitalopram, which comprises purification and optical resolution of 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)benzonitrile to obtain the S-enantiomer, followed by cyclization to give escitalopram with 99.12% purity. The process has the advantages of high yield and high purity.

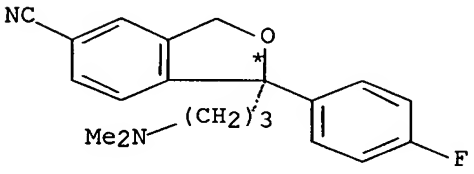
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 1 A ===> B



A

(1)



B

RX(1) RCT A 103146-25-4

STAGE(1)
RGT C 144-62-7 (CO2H)2
SOL 64-17-5 EtOH
CON SUBSTAGE(1) room temperature -> 55 deg C
SUBSTAGE(3) 15 - 20 deg C
SUBSTAGE(4) 4 hours

STAGE(2)
RGT D 7664-41-7 NH3
SOL 108-88-3 PhMe, 7732-18-5 Water
CON 30 - 35 deg C, pH 9.8

STAGE(3)
RGT E 32634-68-7 Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2S,3S)-
SOL 67-63-0 Me2CHOH
CON SUBSTAGE(1) 50 - 55 deg C
SUBSTAGE(3) 25 - 30 deg C
SUBSTAGE(4) 10 hours

STAGE(4)
RGT F 124-63-0 MeSO2Cl, G 121-44-8 Et3N
CON SUBSTAGE(2) 3 hours, -10 - -5 deg C

PRO B 128196-01-0

L7 ANSWER 4 OF 14 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 146:80528 CASREACT Full-text
TITLE: Chemoenzymatic process for the synthesis of escitalopram
INVENTOR(S): Cotticelli, Giovanni; Salvetti, Raul; Bertoni, Chiara
PATENT ASSIGNEE(S): Adorkem Technology SpA, Italy
SOURCE: PCT Int. Appl., 21pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006136521	A1	20061228	WO 2006-EP63193	20060614
WO 2006136521	A8	20070308		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

EP 1736550	A1	20061227	EP 2005-425452	20050622

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU

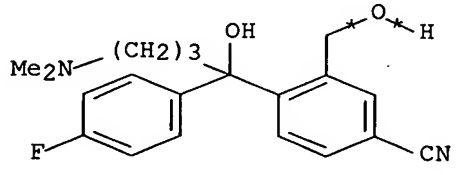
PRIORITY APPLN. INFO.: EP 2005-425452 20050622
US 2005-697398P 20050706

OTHER SOURCE(S): MARPAT 146:80528

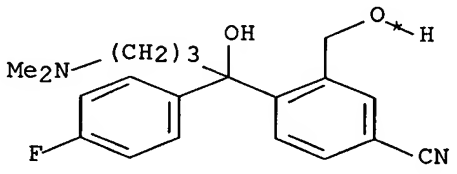
AB A process is described for the preparation of escitalopram and the pharmaceutically acceptable salts thereof starting from 5-cyanophthalide by a process which provides an enantioselective enzymic deacylation reaction of a complex of the formula (IV) where R represents a C1-C4 alkyl residue or an aryl residue under the action of an esterase from Aspergillus niger.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

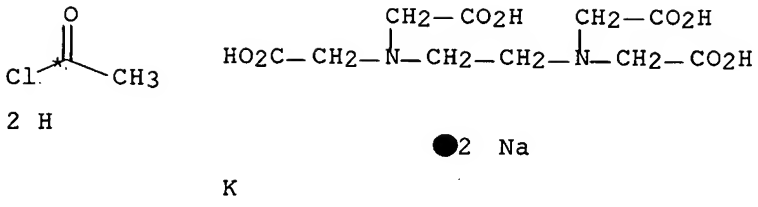
RX(26) OF 27 COMPOSED OF RX(2), RX(3), RX(4), RX(6), RX(7)
RX(26) 2 D + 2 H + K ===> U

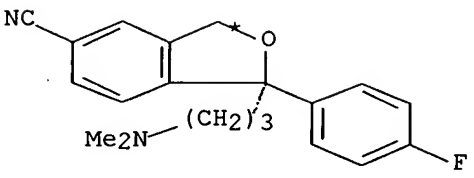


D



D





U

RX(2) RCT D 103146-25-4, H 75-36-5
PRO I 917476-35-8
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 35 - 40 deg C
SUBSTAGE(2) 35 - 40 deg C
NTE hundred gram scale, regioselective

RX(3) RCT I 917476-35-8

STAGE(1)
SOL 64-17-5 EtOH
CON room temperature

STAGE(2)
RCT K 139-33-3
SOL 7732-18-5 Water
CON room temperature

PRO L 917476-34-7
NTE hundred gram scale

RX(4) RCT L 917476-34-7

STAGE(1)
RGT P 7647-01-0 HCl
SOL 64-17-5 EtOH, 7732-18-5 Water
CON room temperature, pH 6

STAGE(2)
CAT 9001-62-1 Lipase
CON room temperature, pH 6

PRO N 917479-14-2, O 674806-13-4
NTE biotransformation, enzymic(lipase from Aspergillus niger immobilized on epoxy resin used), buffered solution(monobasic sodium phosphate), hundred gram scale, stereoselective

RX(6) RCT N 917479-14-2
RGT S 7664-41-7 NH3
PRO R 674806-14-5
SOL 7732-18-5 Water, 67-56-1 MeOH
CON 3 hours, room temperature
NTE gram scale

RX(7) RCT R 674806-14-5

STAGE(1)
RGT V 124-63-0 MeSO2Cl
SOL 108-88-3 PhMe
CON 10 minutes, 0 deg C

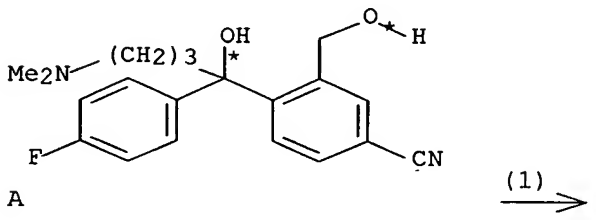
STAGE(2)
RGT W 121-44-8 Et3N
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO U 128196-01-0
NTE alternative preparation shown, gram scale

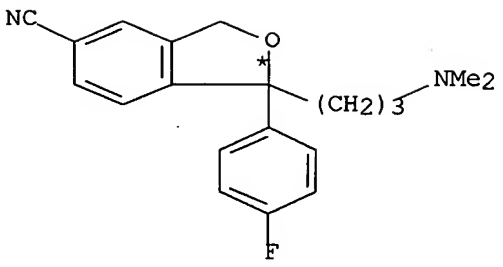
L7 ANSWER 5 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 145:335870 CASREACT Full-text
TITLE: Synthesis of citalopram hydrobromide
AUTHOR(S): Wu, Qiuye; Liao, Hongli; Zhao, Huiqing; Ye, Guangming; Jin, Yongsheng
CORPORATE SOURCE: School of Pharmacy, Second Military Medical University, Shanghai, 200433, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (2005), 36(1), 6-8
CODEN: ZYGZEA; ISSN: 1001-8255
PUBLISHER: Zhongguo Yiyao Gongye Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Citalopram hydrobromide [i.e., 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile monohydrobromide] was synthesized from terephthalic acid and paraformaldehyde by condensation to give 5-carboxyphthalanone, which subjected to condensation, amidation and dehydration to afford 5-cyanophthalanone followed by twice Grignard reaction, cyclization and then salification with an overall yield of 31%.

RX(1) OF 10 ...A ===> B



A



● HBr

B
YIELD 78%

RX(1) RCT A 103146-25-4

STAGE(1)
RGT C 7664-93-9 H2SO4
SOL 7732-18-5 Water, 108-88-3 PhMe
CON SUBSTAGE(1) heated
SUBSTAGE(2) 3 hours, 80 deg C

STAGE(2)
RGT D 1336-21-6 NH4OH
SOL 7732-18-5 Water
CON room temperature, pH 10

STAGE(3)
RGT E 10035-10-6 HBr
CON cooled, pH 6 - 7

PRO B 59729-32-7
NTE HBr gas used in stage 3, overall yield 31%

L7 ANSWER 6 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 145:103520 CASREACT Full-text
TITLE: Preparation and purification of Citalopram salts
INVENTOR(S): Liu, Zhiping; Huang, Weipeng; Yuan, Aiguo; Xiao, Keqiang; Li, Youcheng; Zhuang, Jingfa
PATENT ASSIGNEE(S): Guangdong Xilong Chemical Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 9 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

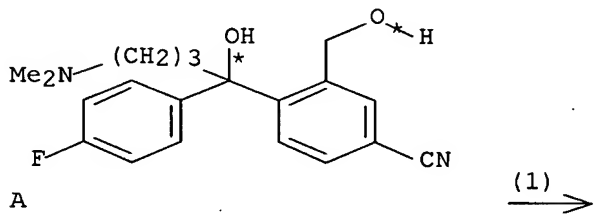
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1740167	A	20060301	CN 2005-10035699	20050712

PRIORITY APPLN. INFO.: CN 2005-10035699 20050712

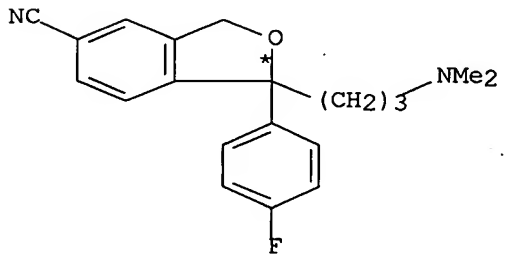
AB The invention provides a method for the preparation and purification of Citalopram salts, which comprises mixing an acid and Citalopram diol compound

at molar ratio of (1-10):1 in toluene at 50-100° under stirring, and recrystg. in water and the diluted acid to obtain corresponding Citalopram salts with a purity above 99.5%; wherein the acid can be hydrobromic acid, hydrochloric acid, hydroiodic acid, hydrofluoric acid, p-toluenesulfonic acid, methylsulfonic acid, oxalic acid, formic acid, acetic acid, hydroxyacetic acid, tartaric acid, citric acid, malic acid, malonic acid, succinic acid, glutaric acid or adipic acid.

RX(1) OF 2 A ===> B



A



● HBr

B
YIELD 91%

RX(1) RCT A 103146-25-4

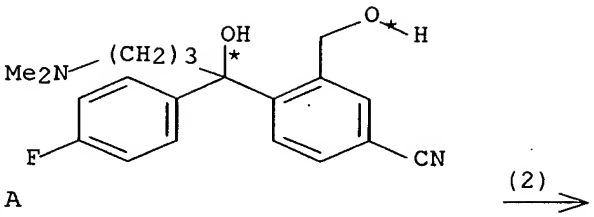
STAGE(1)
RGT C 10035-10-6 HBr
SOL 7732-18-5 Water
CON 90 deg C

STAGE(2)
SOL 141-78-6 AcOEt
CON 3 hours

STAGE(3)
SOL 7732-18-5 Water

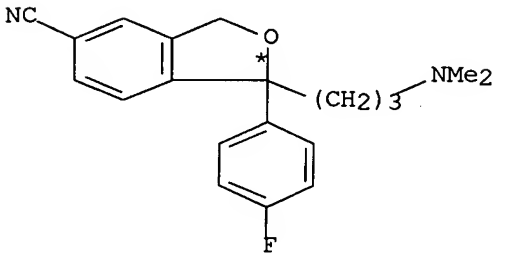
PRO B 59729-32-7
NTE second stage petroleum ether used

RX(2) OF 2 A ===> B



A

(2) →



● HBr

B
YIELD 92%

RX(2) RCT A 103146-25-4

STAGE(1)
RGT C 10035-10-6 HBr
SOL 7732-18-5 Water, 108-88-3 PhMe
CON 90 deg C

STAGE(2)
SOL 141-78-6 AcOEt
CON 3 hours

STAGE(3)
SOL 7732-18-5 Water

PRO B 59729-32-7
NTE second stage petroleum ether used

L7 ANSWER 7 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 144:390731 CASREACT Full-text
TITLE: Intramolecular cyclocondensation process for the preparation of citalopram and escitalopram
INVENTOR(S): Cotticelli, Giovanni; Salvetti, Raul
PATENT ASSIGNEE(S): Adorkem Technology SpA, Italy
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006037714	A2	20060413	WO 2005-EP54566	20050914
WO 2006037714	A3	20060727		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2581195	A1	20060413	CA 2005-2581195	20050914
EP 1794140	A2	20070613	EP 2005-789627	20050914

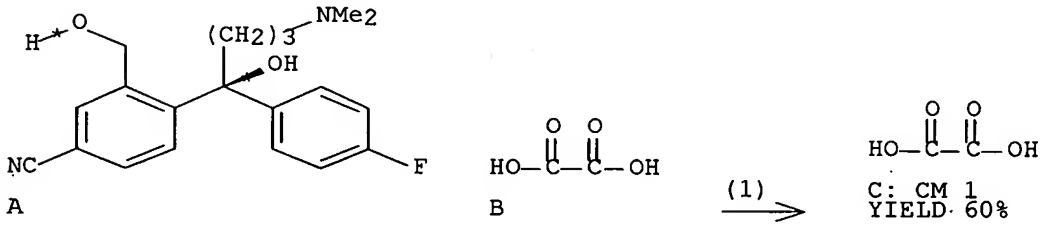
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU

IN 2007DN02442	A	20070504	IN 2007-DN2442	20070330
PRIORITY APPLN. INFO.:			IT 2004-MI1872	20041001
			WO 2005-EP54566	20050914

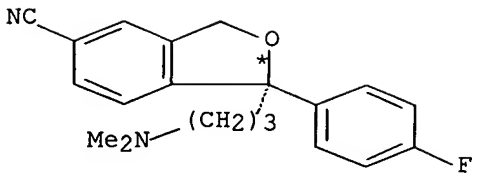
OTHER SOURCE(S): MARPAT 144:390731

AB A process is described for the preparation of citalopram and of the enantiomer escitalopram which comprises the intramol. cyclocondensation of the corresponding glycol or its chiral enantiomer using the Mitsunobu reaction with an azodicarboxylate diester, a phosphine, and a strong base.

RX(1) OF 2 A + B ===> C



A B C: CM 1
YIELD 60%



C: CM 2
YIELD 60%

RX(1) RCT A 488787-59-3

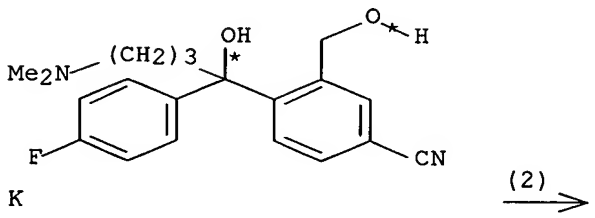
STAGE(1)
RGT D 1972-28-7 EtO2CN:NCO2Et, E 603-35-0 PPh3, F 865-48-5 NaOBu-t
SOL 109-99-9 THF
CON SUBSTAGE(2) overnight

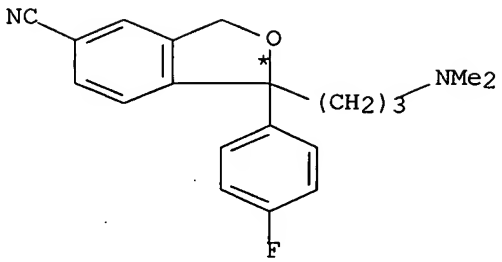
STAGE(2)
RGT G 7647-01-0 HCl
SOL 7732-18-5 Water

STAGE(3)
RCT B 144-62-7
SOL 67-64-1 Me2CO

PRO C 219861-08-2

RX(2) OF 2 K ===> L





● HBr

L
YIELD 42%

RX(2) RCT K 103146-25-4

STAGE(1)
RGT D 1972-28-7 EtO2CN:NCO2Et, E 603-35-0 PPh3, F 865-48-5 NaOBu-t
SOL 109-99-9 THF
CON SUBSTAGE(2) overnight

STAGE(2)
RGT G 7647-01-0 HCl
SOL 7732-18-5 Water

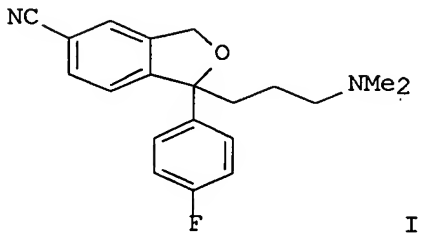
STAGE(3)
RGT M 10035-10-6 HBr
SOL 67-64-1 Me2CO
CON pH 1

PRO L 59729-32-7

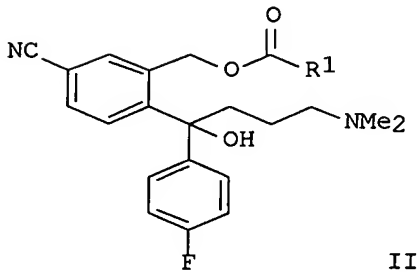
L7 ANSWER 8 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 144:331251 CASREACT Full-text
TITLE: Chemoenzymatic synthesis of (+)-citalopram and (-)-citalopram by kinetic resolution of diol and diol monoester intermediates using esterification or hydrolysis in the presence of Candida antarctica lipase B
INVENTOR(S): Bayod Jasanada, Miguel; Llorente Garcia, Isidro; Gotor Santamaria, Vicente; Brieva Collado, M. Rosario; Fernandez Solares, Laura; Quiros Alvarez, Margarita
PATENT ASSIGNEE(S): Astur Pharma, S.A., Spain; Universidad de Oviedo
SOURCE: Span., 14 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2228274	A1	20050401	ES 2003-2215	20030924
ES 2228274	B1	20060601		

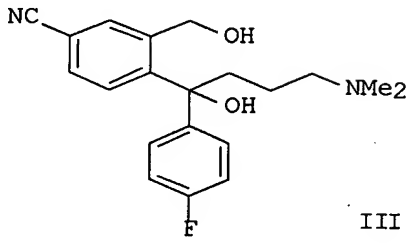
PRIORITY APPLN. INFO.: ES 2003-2215 20030924
OTHER SOURCE(S): MARPAT 144:331251
GI



I

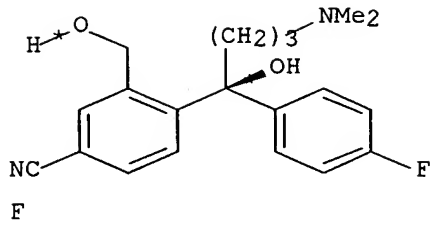


II



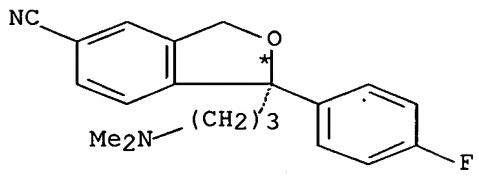
III

AB New processes and intermediates for the preparation of (S)-(+)- and (R)-(-)-citalopram, i.e., (+)- and (-)-I, are disclosed. The claimed intermediates include the optically enriched diol monoesters (+)- and (-)-II, as well as the diols (+)- and (-)-III [wherein: R1 = alkyl or aryl]. The claimed processes include two types of kinetic resolution: (1) enzymic acylation of racemic diol (±)-III with an acylating agent R1CO2R2 [R1 = alkyl or aryl; R2 = alkyl, alkenyl or aryl], to give (R)-(+)-II and (S)-(-)-III; and (2) enzymic hydrolysis of the racemic ester (±)-II, to give (S)-(-)-II and (R)-(+)-III. The enzyme catalyst is a hydrolase, especially a lipase, and most particularly, fraction B of the lipase of Candida antarctica (IV). Five examples are given; these cover both of the aforementioned processes, as well as hydrolysis of a monoester resolution product, and the conversion of both III enantiomers to the corresponding I enantiomers. For instance, reaction of (±)-III with vinyl acetate in MeCN in the presence of immobilized IV at 30° for 20 h gave (S)-(-)-III in 47% yield and >99% enantiomeric excess, along with some (R)-(+)-II (R1 = Me) with >90% ee. Cyclization of (S)-(-)-III by slow treatment with mesyl chloride in CH2Cl2 at 0°, followed by stirring for 1 h at 15°, gave (S)-(+)-I in 90% yield and >99% ee.



F

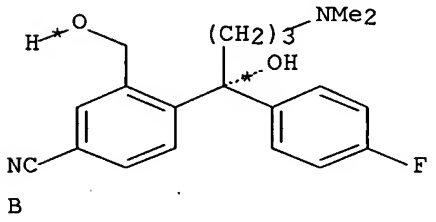
(2) →



G
YIELD 90%

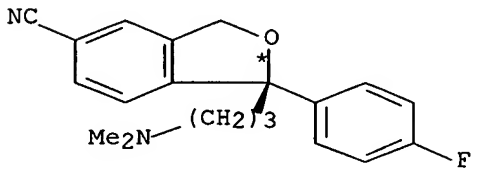
RX(2)
RCT F 488787-59-3
RGT H 124-63-0 MeSO2Cl
PRO G 128196-01-0
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 0 deg C -> 15 deg C
SUBSTAGE(3) 1 hour, 15 deg C
NTE product ee >99%

RX(3) OF 10 ...B ===> J



B

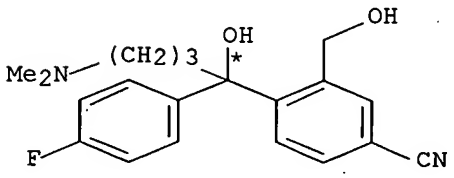
(3) →



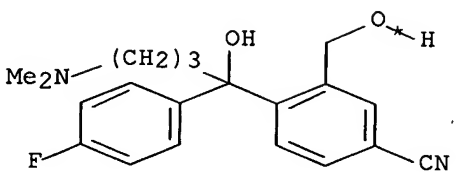
J
YIELD 90%

RX(3) RCT B 481047-48-7
       RGT H 124-63-0 MeSO2Cl
       PRO J 128196-02-1
       SOL 75-09-2 CH2Cl2
       CON SUBSTAGE(1) 0 deg C
            SUBSTAGE(2) 0 deg C -> 15 deg C
            SUBSTAGE(3) 1 hour, 15 deg C
       NTE product ee >99%

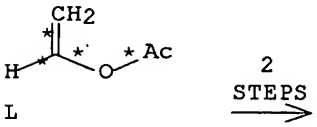
RX(9) OF 10 COMPOSED OF RX(4), RX(2)
RX(9) 2 K + L ===> G



K

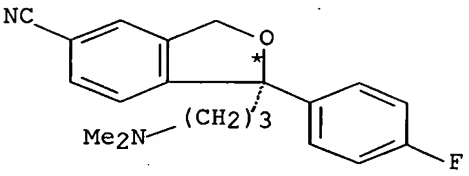


K



L

2
STEPS



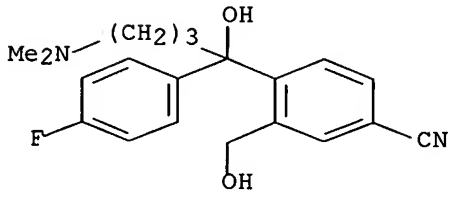
G
YIELD 90%

RX(4) RCT K 103146-25-4, L 108-05-4
       PRO A 674806-13-4, F 488787-59-3
       CAT 9001-62-1 Lipase
       SOL 75-05-8 MeCN
       CON 20 hours, 30 deg C
       NTE enzymic, solid-supported catalyst, ee of diol >99%, ee of monoester >90%

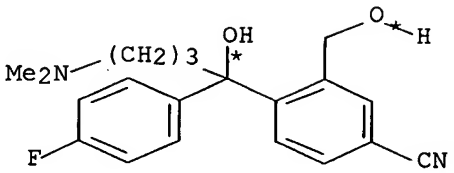
RX(2) RCT F 488787-59-3
       RGT H 124-63-0 MeSO2Cl
       PRO G 128196-01-0
       SOL 75-09-2 CH2Cl2
       CON SUBSTAGE(1) 0 deg C

SUBSTAGE(2) 0 deg C -> 15 deg C
SUBSTAGE(3) 1 hour, 15 deg C
NTE product ee >99%

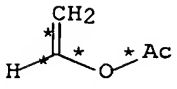
RX(10) OF 10 COMPOSED OF RX(4), RX(1), RX(3)
RX(10) 2 K + L ===> J



K

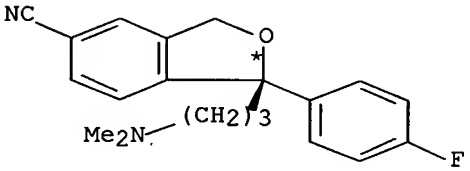


K



L

3
STEPS



J
YIELD 90%

RX(4) RCT K 103146-25-4, L 108-05-4
PRO A 674806-13-4, F 488787-59-3
CAT 9001-62-1 Lipase
SOL 75-05-8 MeCN
CON 20 hours, 30 deg C
NTE enzymic, solid-supported catalyst, ee of diol >99%, ee of monoester >90%

RX(1) RCT A 674806-13-4
RGT C 7732-18-5 Water, D 1310-73-2 NaOH
PRO B 481047-48-7
SOL 67-56-1 MeOH
CON 12 hours, room temperature
NTE ee of product >99%

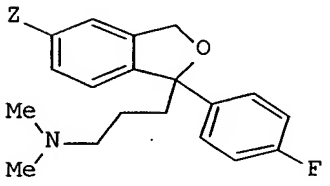
RX(3) RCT B 481047-48-7
RGT H 124-63-0 MeSO2Cl
PRO J 128196-02-1
SOL 75-09-2 CH2Cl2

CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 0 deg C -> 15 deg C
SUBSTAGE(3) 1 hour, 15 deg C
NTE product ee >99%

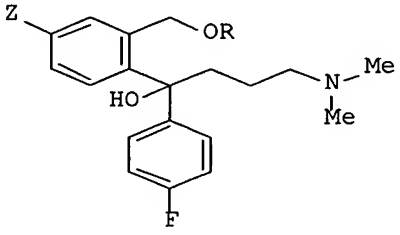
L7 ANSWER 9 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 144:274127 CASREACT Full-text
TITLE: Process for preparation of citalopram and its enantiomers via acid or base cyclization of the diol
INVENTOR(S): Periyandi, Nagarajan; Kilaru, Srinivasu; Thennati, Rajamannar
PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Limited, India
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006021971	A2	20060302	WO 2005-IN276	20050812
WO 2006021971	A3	20060713		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
IN 2004MU00912	A	20070420	IN 2004-MU912	20040823
EP 1797060	A2	20070620	EP 2005-815687	20050812
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.: IN 2004-MU912 20040823
WO 2005-IN276 20050812
OTHER SOURCE(S): MARPAT 144:274127
GI



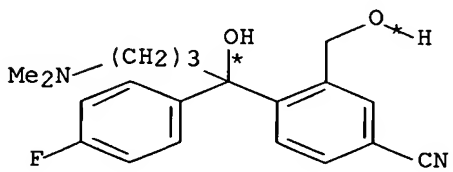
I



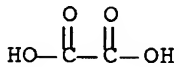
II

AB The invention provides a process for preparation of 1-[3-(dimethylamino)propyl]- 1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile I (Z = CN; citalopram) and its enantiomers. The process for preparation of compound I comprising reacting a compound of formula II (R = H), in the presence of a base, with a compound of formula RX, wherein R is (un)substituted alkyl, (un)substituted alkenyl, and (un)substituted (hetero)aryl; X is from F, Cl, Br, I, CN, OTf and OR1; R1 is (un)substituted alkyl; Z is CN or a group that may be converted to a cyano group; so that an intermediate ether derivative, where R is as defined above, is formed from said reaction, which ether cyclizes to give a compound of formula I, where Z is not a cyano group, and conversion of the group Z in the compound of formula I to a cyano group to form racemic I (Z = CN), is claimed in this invention. The invention also provides ether compds., compds. of formula II and a process for preparation thereof. (S)-(+)-Citropram, i.e., (S)-(+)-I (Z = CN) was prepared by nucleophilic aromatic substitution of 2,5-dichloronitrobenzene with (S)-(-)-II (Z = CN; R = H) to give the corresponding benzylic Ph ether, that was converted to its HCl salt, and cyclized in the presence of potassium carbonate to give (S)-(+)-I.

RX(1) OF 9 A + B ===> C

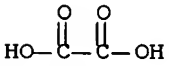


A

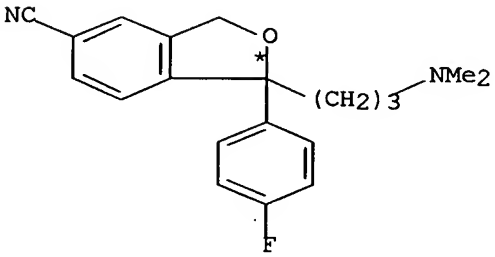


B

(1) ⟶



C: CM 1



C: CM 2

RX(1) RCT A 103146-25-4

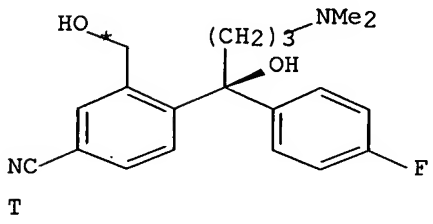
STAGE(1)
RGT D 89-61-2 Benzene, 1,4-dichloro-2-nitro-, E 584-08-7 K2CO3
SOL 67-68-5 DMSO
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 15 hours, 100 deg C

STAGE(2)
RGT F 1310-73-2 NaOH, G 12408-02-5 H+
SOL 7732-18-5 Water

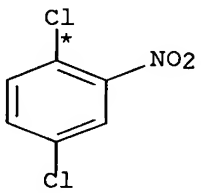
STAGE(3)
RCT B 144-62-7
SOL 67-64-1 Me2CO
CON SUBSTAGE(1) 30 deg C
SUBSTAGE(2) cooled

PRO C 207559-01-1

RX(9) OF 9 COMPOSED OF RX(6), RX(4), RX(5)
RX(9) T + D ===> S

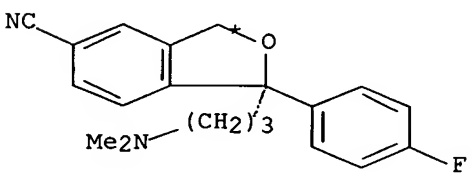


T



D

3 STEPS



S

RX(6) RCT T 488787-59-3

STAGE(1)
RGT M 865-47-4 t-BuOK
SOL 109-99-9 THF
CON 10 minutes, 0 - 10 deg C

STAGE(2)
RCT D 89-61-2
CON SUBSTAGE(1) 0 - 10 deg C
SUBSTAGE(2) 10 - 15 hours, 30 - 35 deg C

STAGE(3)
RGT F 1310-73-2 NaOH
SOL 7732-18-5 Water

PRO O 878042-63-8

RX(4) RCT O 878042-63-8
RGT Q 7647-01-0 HCl
PRO P 878007-22-8
SOL 67-63-0 Me2CHOH
CON 30 deg C

RX(5) RCT P 878007-22-8
RGT E 584-08-7 K2CO3
PRO S 128196-01-0
SOL 67-68-5 DMSO
CON SUBSTAGE(1) 30 - 35 deg C
SUBSTAGE(2) 30 minutes, 95 - 100 deg C

L7 ANSWER 10 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 143:248161 CASREACT Full-text
TITLE: Method for the separation of intermediates which may be used for the preparation of escitalopram
INVENTOR(S): Lyngso, Lars Ole
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005077891	A1	20050825	WO 2005-DK75	20050202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005212455	A1	20050825	AU 2005-212455	20050202
CA 2555980	A1	20050825	CA 2005-2555980	20050202
EP 1716108	A1	20061102	EP 2005-700625	20050202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
CN 1918112	A	20070221	CN 2005-80004594	20050202
BR 2005007580	A	20070731	BR 2005-7580	20050202
JP 2007524678	T	20070830	JP 2006-552461	20050202
MX 2006PA08977	A	20061020	MX 2006-PA8977	20060808
IN 2006CN02945	A	20070608	IN 2006-CN2945	20060810
NO 2006004086	A	20060912	NO 2006-4086	20060912

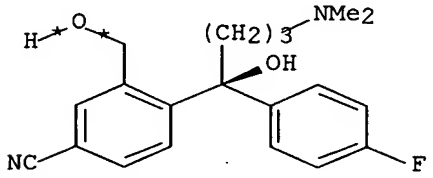
US 2007190624 A1 20070816 US 2006-597836 20061108
PRIORITY APPLN. INFO.: DK 2004-217 20040212
US 2004-544970P 20040212
WO 2005-DK75 20050202
OTHER SOURCE(S): MARPAT 143:248161
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

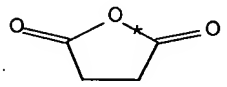
AB Compds. I [R1 = H, or group II; R2 = CN, or a group which may be converted to CN; R3 = halo; X = double or single bond; Y = bond, O, S, or NH; W = O, or S; R4 = alkyl, alkenyl, alkynyl, aryl, hetroaryl, all of which may be optionally substituted with alkoxy, alkythio, halo, OH, NH, NO2, CN, alkylamino, aryl, aryloxy, arylthio, and heteroaryl], or a salt from a mixture of I [R1 = group II] and I [R1 = H], which was reacting with cyclic anhydride or imide to form a mixture of I [R1 = group II] and an esters III (R5 = substituted heteroaryl carboxylic acid), were prepared by enzymic acylation or deacylation, separated, isolated and purified and used for manufacturing of escitalopram and derivs. Compds. I [R1 = group II] were separated from esters III by precipitation of III from the mixture, or by partitioning between an organic solvent and aqueous solvent, by adsorbing I [R1 = group II] on a basic resin. Thus, addition of succinic anhydride to a mixture of butyric acid 5-cyano-2-[4-dimethylamino-1-(4-fluorophenyl)-1-hydroxybutyl]-benzyl ester and prepared by enzymic resolution 4-[(S)-4-dimethylamino-1-(4'-fluorophenyl)-1-hydroxybutyl]-3-hydroxymethylbenzonitrile, gave after precipitation and washing 2,02 g of escitalopram [(S)-1-(3-dimethylamino-propyl)-1-(4-fluoro-phenyl)- 1,3-dihydro-isobenzofuran-5-carbonitrile] hydrogen oxalate (ee = 95%).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

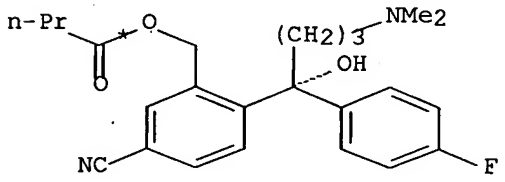
RX(4) OF 6 COMPOSED OF RX(1), RX(2)
RX(4) A + 2 B + C + F ===> G



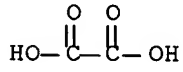
A



2 B

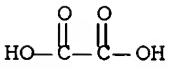


C

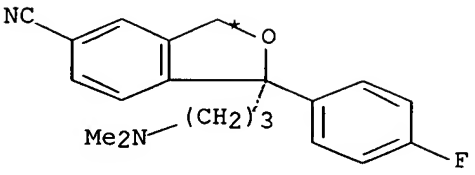


F

2 STEPS →



G: CM 1



G: CM 2

RX(1) RCT A 488787-59-3, B 108-30-5, C 658080-70-7
PRO D 863116-45-4
SOL 109-99-9 THF
CON overnight, room temperature

RX(2) RCT D 863116-45-4

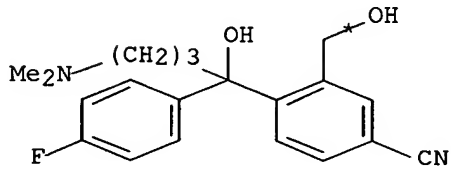
STAGE(1)
RGT H 7646-69-7 NaH
SOL 68-12-2 DMF
CON overnight, room temperature

STAGE(2)
RGT I 7732-18-5 Water
CON room temperature

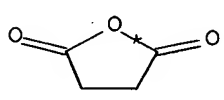
STAGE(3)
RCT F 144-62-7
SOL 67-64-1 Me2CO
CON 1 hour, room temperature

PRO G 219861-08-2

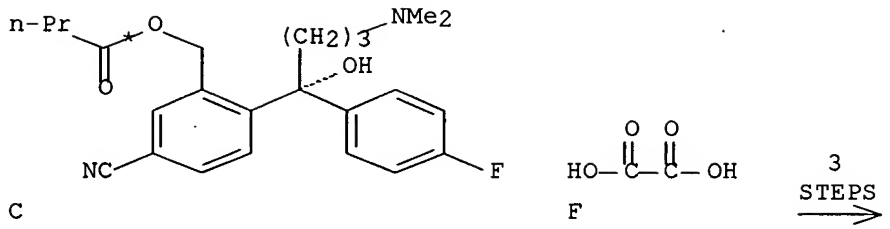
RX(6) OF 6 COMPOSED OF RX(3), RX(1), RX(2)
RX(6) L + 2 B + C + F ===> G



L



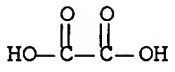
2 B



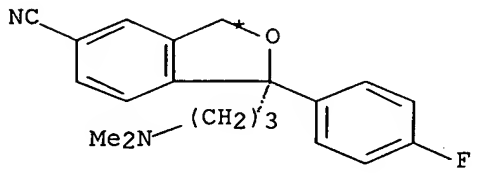
C

F

3 STEPS



G: CM 1



G: CM 2

RX(3) RCT L 103146-25-4
RGT M 123-20-6 Butanoic acid, ethenyl ester
PRO A 488787-59-3
CAT 9004-02-8 Lipase, lipoprotein
SOL 123-91-1 Dioxane
CON SUBSTAGE(1) room temperature -> 50 deg C
SUBSTAGE(2) 192 hours, 50 deg C
SUBSTAGE(3) 504 hours, 50 deg C
NTE biotransformation, enzymic, stereoselective, lipoptrotein lipase from Pseudomonas sp. used

RX(1) RCT A 488787-59-3, B 108-30-5, C 658080-70-7
PRO D 863116-45-4
SOL 109-99-9 THF
CON overnight, room temperature

RX(2) RCT D 863116-45-4

STAGE(1)
RGT H 7646-69-7 NaH
SOL 68-12-2 DMF
CON overnight, room temperature

STAGE(2)
RGT I 7732-18-5 Water
CON room temperature

STAGE(3)

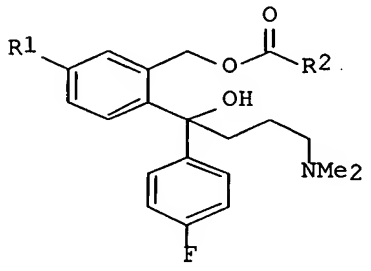
RCT F 144-62-7
SOL 67-64-1 Me2CO
CON 1 hour, room temperature

PRO G 219861-08-2

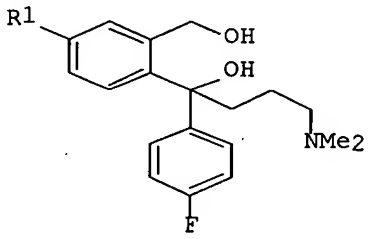
L7 ANSWER 11 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 143:59681 CASREACT Full-text
TITLE: Process for the preparation of citalopram enantiomer
INVENTOR(S): Li, Lan; Li, Qian
PATENT ASSIGNEE(S): Dezhong Wanquan Pharmaceutical Technology Developing Co., Ltd., Beijing, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, No pp. given
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1510024	A	20040707	CN 2002-158181	20021224
PRIORITY APPLN. INFO.:			CN 2002-158181	20021224

OTHER SOURCE(S): MARPAT 143:59681
GI



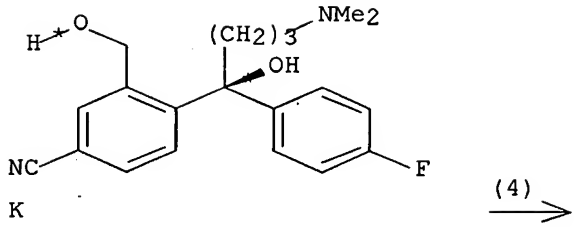
I



II

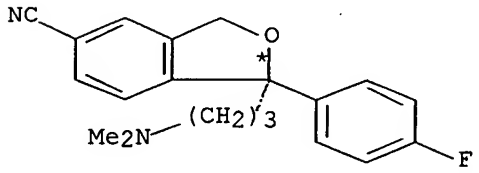
AB A process for the preparation of title compound, a drug as antidepressant, and the preparation of its intermediate I [R1 = CN, halo, alkoxy, alkylaminocarbonyl; R2 = amino containing group, amino containing aryl or cyclic ring] comprising reacting a compound of formula II with a compound of formula XCOR2 (R1, R2 are defined as above) is disclosed. For example, reaction of II (R1 = CN) with 2-chloronicotinic acid gave I (R1 = CN, R2 = 2-chloropyridin-3-yl) in 80% yield. Optical resolution of I by salification of I with di-p-toluoyl-L-tartaric acid , followed by recrystn. and hydrolysis, provided (S)-II. Cyclization of (S)-II gave optical active (S)-citalopram.

RX(4) OF 10 ...K ===> P



K

(4) ⟶



P

RX(4) RCT K 488787-59-3

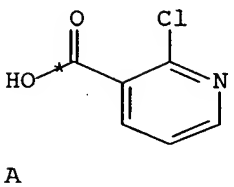
STAGE(1)
RGT D 121-44-8 Et3N
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)
RGT Q 98-59-9 TsCl
SOL 75-09-2 CH2Cl2
CON 3 hours, 0 deg C

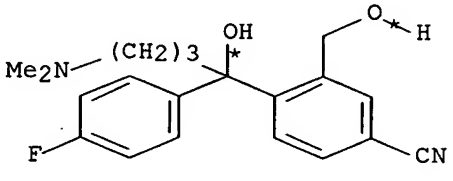
STAGE(3)
RGT R 144-62-7 (CO2H)2
SOL 67-64-1 Me2CO
CON SUBSTAGE(1) 1 hour, reflux
SUBSTAGE(2) overnight, reflux -> room temperature

PRO P 128196-01-0

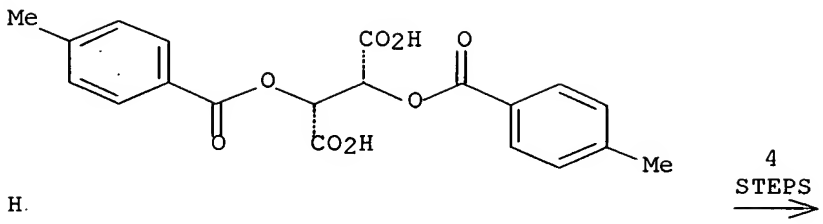
RX(10) OF 10 COMPOSED OF RX(1), RX(2), RX(3), RX(4)
RX(10) A + B + H ===> P



A

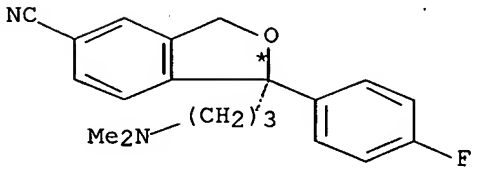


B



H

4 STEPS



P

RX(1) RCT A 2942-59-8

STAGE(1)
SOL 7719-09-7 SOCl2
CON 2 hours, reflux

STAGE(2)
RCT B 103146-25-4
SOL 75-09-2 CH2Cl2

STAGE(3)
RGT D 121-44-8 Et3N
CON 16 hours, room temperature

STAGE(4)
SOL 108-20-3 Isopropyl ether
CON 2 hours, room temperature

PRO C 853904-55-9

RX(2) RCT C 853904-55-9, H 32634-66-5
PRO I 853904-57-1
SOL 67-63-0 Me2CHOH
CON SUBSTAGE(1) 0.5 hours, reflux
SUBSTAGE(2) overnight, reflux -> room temperature
NTE stereoselective

RX(3) RCT I 853904-57-1

STAGE(1)
RGT L 497-19-8 Na2CO3
SOL 7732-18-5 Water
CON room temperature, pH 8 - 9

STAGE(2)

SOL 108-20-3 Isopropyl ether
CON 2 hours, room temperature

STAGE(3)
RGT M 1310-73-2 NaOH
SOL 7732-18-5 Water, 64-17-5 EtOH
CON 8 hours, room temperature

PRO K 488787-59-3

RX(4) RCT K 488787-59-3

STAGE(1)
RGT D 121-44-8 Et3N
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)
RGT Q 98-59-9 TsCl
SOL 75-09-2 CH2Cl2
CON 3 hours, 0 deg C

STAGE(3)
RGT R 144-62-7 (CO2H)2
SOL 67-64-1 Me2CO
CON SUBSTAGE(1) 1 hour, reflux
SUBSTAGE(2) overnight, reflux -> room temperature

PRO P 128196-01-0

L7 ANSWER 12 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 142:197860 CASREACT Full-text
TITLE: Process for purification of citalopram via washing with polybasic acid solutions
INVENTOR(S): Uttarwar, Sunil Govindrao; Gawli, Bhagwan Narayan
PATENT ASSIGNEE(S): Meditab Specialities Pvt. Ltd., India; Wain, Christopher Paul
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

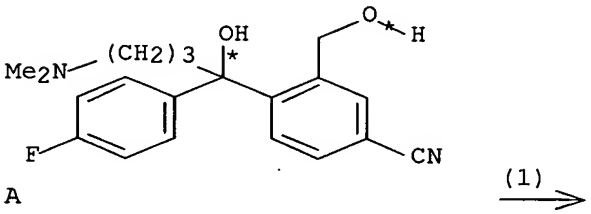
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005012278	A2	20050210	WO 2004-GB3209	20040723
WO 2005012278	A3	20050616		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

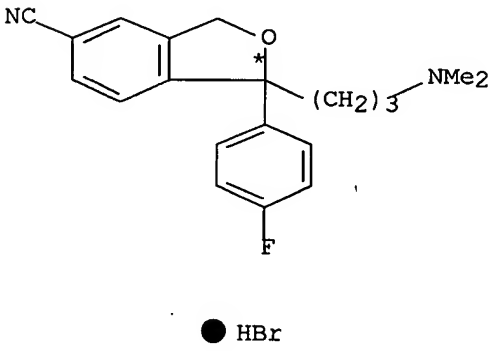
GB 2418916	A	20060412	GB 2006-1023	20040723
DE 112004001368	T5	20060629	DE 2004-112004001368	20040723
IN 2006MN00092	A	20061006	IN 2006-MN92	20060124
US 2006189816	A1	20060824	US 2006-565736	20060419
PRIORITY APPLN. INFO.:			GB 2003-17475	20030725
			WO 2004-GB3209	20040723

AB A process for purification of racemic or optically active citalopram (I) comprises (i) providing crude I containing ≥1 I derivs. dissolved in a H2O-immiscible organic solvent, (ii) washing the crude mixture with ≥1 dilute aqueous solution of a polybasic acid, either in free form or as a partial alkali metal salt, so as to sep. I from impurities present in the crude mixture; and (iii) where required converting purified I free base to a pharmaceutically acceptable salt. Thus, 4-[4-(dimethylamino)-1-(4'-fluorophenyl)-1-hydroxybutyl]-3-hydroxymethylbenzonitrile was heated at 105° in aqueous H3PO4 followed by cooling, dilution with H2O, pH adjustment to 8-10 with aqueous NH3, and extraction with EtOAc. The EtOAc layer was washed with aqueous disodium edetate followed by drying over Na2SO4, treatment with decolorizing C, and filtration to give >99.85% pure citalopram hydrobromide.

RX(1) OF 3 A ===> B



A



B

RX(1) RCT A 103146-25-4

STAGE(1)
RGT C 7664-38-2 H3PO4
SOL 7732-18-5 Water

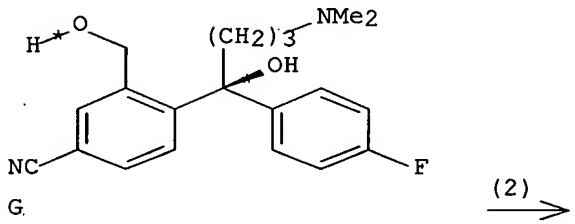
CON 14 hours, 105 deg C

STAGE(2)
RGT D 7664-41-7 NH3
SOL 7732-18-5 Water
CON 40 deg C, pH 8 - 10

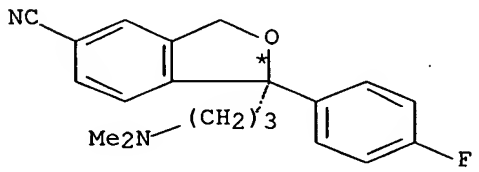
STAGE(3)
RGT E 10035-10-6 HBr
SOL 7732-18-5 Water
CON room temperature, pH 3 - 3.5

PRO B 59729-32-7

RX(2) OF 3 G ===> H



G



H

RX(2) RCT G 488787-59-3

STAGE(1)
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)
RGT I 124-63-0 MeSO2Cl, J 121-44-8 Et3N
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 2 hours, 5 deg C

STAGE(3)
RGT K 144-62-7 (CO2H)2
SOL 67-64-1 Me2CO
CON 1 hour, 10 deg C

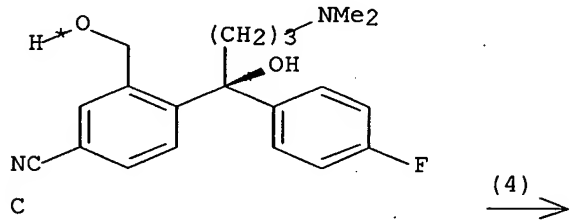
PRO H 128196-01-0

L7 ANSWER 13 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 140:287145 CASREACT Full-text
TITLE: Enzymatic resolution of a quaternary stereogenic center as the key step in the synthesis of (S)-(+)-citalopram
AUTHOR(S): Solares, Laura F.; Brieva, Rosario; Quiros, Margarita; Llorente, Isidro; Bayod, Miguel; Gotor, Vicente
CORPORATE SOURCE: Departamento de Quimica Organica e Inorganica, Facultad de Quimica, Universidad de Oviedo, Oviedo, 33071, Spain
SOURCE: Tetrahedron: Asymmetry (2004), 15(2), 341-345
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

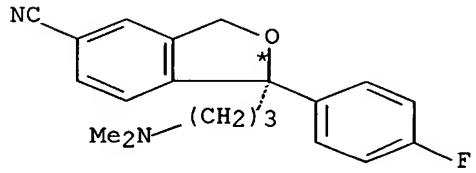
AB The enzymic resolution of 4-[4-(Dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)benzonitrile, a useful intermediate in the synthesis of enantiomerically pure citalopram, has been studied. Candida antarctica lipase B (CAL-B) catalyzes the enzymic acetylation of the primary benzylic alc. with high enantioselectivity at the quaternary stereogenic center. This enzymic acetylation yielded the acetylated (+)-3-[(acetyloxy)methyl]-4-[(1R)-4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]benzonitrile and the desired (-)-4-[(1S)-4-(dimethylamino)-1- (4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)benzonitrile. The enzymic enantioselective hydrolysis of the 3-acetyloxymethyl derivative catalyzed by CAL-B is also possible.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(4) OF 6 ...C ===> N



C

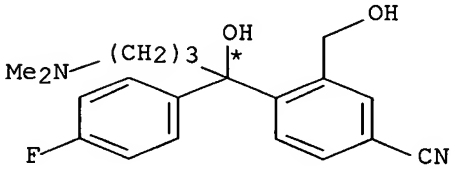


N
YIELD 90%

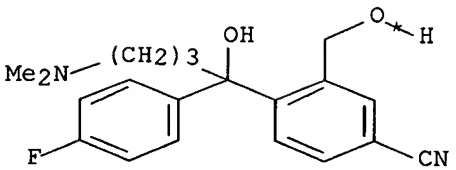
RX(4) RCT C 488787-59-3
RGT O 124-63-0 MeSO2Cl
PRO N 128196-01-0

SOL 75-09-2 CH2Cl2
CON 1 hour, 0 deg C -> 15 deg C

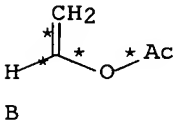
RX(6) OF 6 COMPOSED OF RX(1), RX(4)
RX(6) 2 A + B ===> N



A

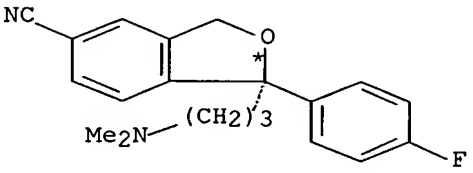


A



B

2
STEPS



N
YIELD 90%

RX(1) RCT A 103146-25-4, B 108-05-4
PRO C 488787-59-3, D 674806-13-4
CAT 9001-62-1 Lipase
SOL 75-05-8 MeCN
CON 21 hours, 30 deg C
NTE biotransformation, enzymic, stereoselective, lipase B from Candida antarctica, optimization study, optimized on concentration,solvent

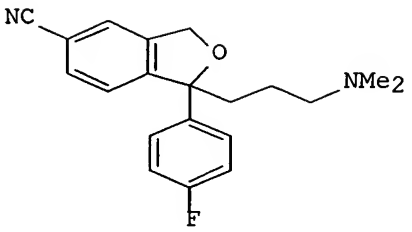
RX(4) RCT C 488787-59-3
RGT O 124-63-0 MeSO2Cl
PRO N 128196-01-0
SOL 75-09-2 CH2Cl2
CON 1 hour, 0 deg C -> 15 deg C

L7 ANSWER 14 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 138:73169 CASREACT Full-text
TITLE: Preparation of racemic citalopram and/or S- or R-citalopram by separation of a mixture of R- and S-citalopram

INVENTOR(S): Humble, Rikke Eva; Christensen, Troels Volsgaard; Rock, Michael Harold; Nielsen, Ole; Petersen, Hans; Dancer, Robert
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000672	A1	20030103	WO 2002-DK426	20020625
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EG 22991	A	20031231	EG 2002-725	20020624
CA 2450890	A1	20030103	CA 2002-2450890	20020625
AU 2002344948	A1	20030108	AU 2002-344948	20020625
AU 2002344948	B2	20070816		
EP 1412341	A1	20040428	EP 2002-742848	20020625
EP 1412341	B1	20041208		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002010574	A	20040803	BR 2002-10574	20020625
CN 1520405	A	20040811	CN 2002-812668	20020625
HU 200400293	A2	20040928	HU 2004-293	20020625
HU 200400293	A3	20070529		
JP 2004536093	T	20041202	JP 2003-507077	20020625
AT 284395	T	20041215	AT 2002-742848	20020625
PT 1412341	T	20050429	PT 2002-742848	20020625
ES 2233834	T3	20050616	ES 2002-2742848	20020625
TW 236473	B	20050721	TW 2002-91113845	20020625
NZ 530104	A	20060831	NZ 2002-530104	20020625
ZA 2003009633	A	20041213	ZA 2003-9633	20031211
MX 2003PA11770	A	20040402	MX 2003-PA11770	20031217
BG 108532	A	20050430	BG 2004-108532	20040114
IN 2004CN00142	A	20051209	IN 2004-CN142	20040123
US 2004259940	A1	20041223	US 2004-482000	20040209
US 7112686	B2	20060926		
PRIORITY APPLN. INFO.:			DK 2001-991	20010625
			WO 2002-DK426	20020625

GI

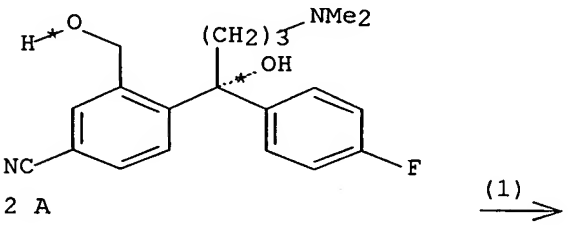


I

AB Citalopram (I), free base or an acid addition salt thereof, and/or R- or S-citalopram as the free base or an acid addition salt thereof, were prepared by separation of a mixture of R- and S-citalopram with more than 50% of one of the enantiomers into a fraction consisting of racemic citalopram and/or a fraction of S-citalopram or R-citalopram. The mixture of R- and S-citalopram was generally prepared by acid- or base-catalyzed ring closure of R- or S-[4-(dimethylamino)-1-(4'-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)benzonitrile. Racemic citalopram and S-citalopram are well-known antidepressants (no data).

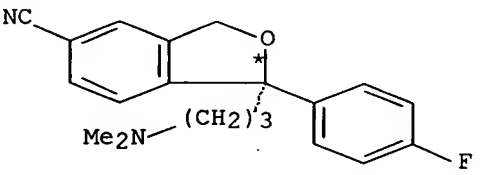
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 1 2 A ===> B + C

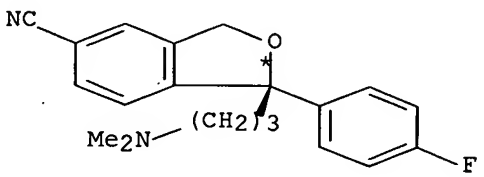


2 A

(1)



B
YIELD 99%(73)



C
YIELD 99%(27)

RX(1) RCT A 481047-48-7
RGT D 7664-93-9 H2SO4
PRO B 128196-01-0, C 128196-02-1
SOL 7732-18-5 Water, 75-05-8 MeCN
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 3 hours, 78 - 85 deg C
NTE optimization study

```
=> save l7 temp cott10577869/a
ANSWER SET L7 HAS BEEN SAVED AS 'COTT10577869/A'

=> logoff h
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY     SESSION
FULL ESTIMATED COST                                  227.42      229.88

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY     SESSION
CA SUBSCRIBER PRICE                                  -10.22      -10.22

 SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 18:54:24 ON 28 SEP 2007
```

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	2744	citalopram	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/28 17:52
L2	34	L1 and (methane adj sulfonyl)	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/28 18:06
L6	494	citalopram and cyclization	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/28 19:04
L7	239	diol and (methane$2sulfonyl$2chloride)	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/28 17:55
L8	495	l6 andl7	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/28 17:55
L9	0	l6 and l7	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/28 17:57
L10	219	"4136193"	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/28 17:57
L11	0	"4136193.pn."	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/28 17:57
L12	4	"4136193".pn.	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/28 17:57

EAST Search History

L13	2	"4,650,884".pn.	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/28 18:19
L14	2	"4943590".pn.	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/28 18:19
L15	97	l6 and triphenylphosphine	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/28 19:05
S1	94	5-cyanophthalide	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/28 17:52
S2	66074	phosphine	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/12 19:51
S3	99	S1 andl2	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/12 19:52
S4	2722	citalopram	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/28 17:54
S5	103	S3 andl4	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/12 19:53
S6	82	S3 and S4	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/12 19:54
S7	51	cotticelli	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/12 19:54

EAST Search History

S8	9	S6 and S7	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/12 19:57
S9	41	5-carboxyphthalide	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/12 19:57
S10	20	S9 and S1	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/09/12 19:57